REMARKS

Claims 1-5, 7-9 and 17-19 are currently pending. Claims 6 and 11 were previously cancelled, and claims 10 and 12-16 are currently cancelled. Claims 1 and 17 are currently amended and support can be found, for example, in Figure 1.

Examiner Interview

Applicants would like to thank Examiner Bowers for the telephonic interview of October 22, 2007. The Examiner agreed that the additional limitation of the channels being formed as through-holes in the top member in amended claims 1 and 17 would overcome the currently pending rejections.

Claim Rejections - 35 U.S.C. 103

Claims 1-5, 7, 9 and 17-19 stand rejected under 35 U.S.C. 103(a) as being allegedly rendered obvious by U.S. Patent No. 6,632,619 to Harrison ("Harrison") in view of U.S. Patent No. 6,238,874 to Jarnigan ("Jarnigan") in further view of U.S. Patent No. 6,705,357 to Jeon ("Jeon"). Neither Harrison, Jarnigan or Jeon, alone or in combination, teach all of the limitations of claim 1. Specifically, independent claim 1 recites that: the housing has a base member and a top member and the at least one channel is formed as a through-hole in the top member; a first fluid stream has a first concentration of a first substance; a second fluid stream has a second concentration of a second substance; and the first fluid stream and the second fluid stream flow adjacent and parallel to each other without mixing, to create a dynamic concentration gradient.

Harrison describes a microfluidic device that comprises a base plate and a cover that is bonded to the base plate. Harrison describes channels etched into the top surface of the base plate, or both the top surface of the base plate and the bottom surface of the cover (col 5, lines 30-37; Example I). Thus, the channels in Harrison are not formed as through-holes in the top member, as recited in claim 1.

Claim 1 further recites that a first fluid stream has a first concentration of a first substance and a second fluid stream has a second concentration of a second substance. The Examiner states that Harrison teaches a first fluid stream (inlet flow path 8') having a first concentration of a first substance and a second fluid stream (inlet flow path 8") having a second concentration of

a second substance. However, 8' and 8" simply represent two channels in the device of Harrison, and Harrison remains silent as to any specific concentration of the substances in these channels. Thus, Harrison does not create a concentration gradient, as recited in claim 1. Furthermore, the fluid streams in Harrison are in distinctly separate channels and are not adjacent or parallel (Fig. 2), as claim 1 recites.

Claim 1 further states that the first fluid stream and the second fluid stream *do not mix*. However, the inlet flow paths of Harrison are intended to intersect and merge with the main flow path. One inlet path contains the cells of interest and a second inlet flow path contains the compound of interest. The cells and the compound mix at the point where the second flow path enters into the main flow path (col 2, lines 38-49). Therefore, the purpose of the inlet channels of Harrison is for the two substances to mix together and the invention would fail to operate as intended if the substances did not mix.

With respect to claim 17, Harrison broadly describes a method to study leukocyte rolling. However, Harrison does not recite the specific method steps of claim 17. Specifically, the Examiner has failed to address the steps of disposing either a leukocyte migration mediator or endothelial cells in the channel and delivering a sample comprising leukocytes to the channel by laminar flow. The Examiner states, "Harrison specifically discloses the presence of endothelial cells and various mediators such as selectins and cytokines," however the mere presence of these cells is not what is claimed; these cells must be disposed in a specific location in the device.

With respect to claim 1, Jarnigan fails to cure the deficiencies of Harrison. Jarnigan describes a channel region in Fig. 5B, which is relied upon for the examiner's rejection. Although Jarnigan discloses a base member (8) and a top cover (10) in Fig. 1, the configuration of a support member and a top member is not contemplated by Jarnigan for the embodiment of Fig. 5B and there is no motivation or suggestion to add such a support member and top member to the embodiment depicted in Fig. 5B. In other words, Jarnigan's embodiment of Fig. 1 cannot be combined with the embodiment of Fig. 5 in the way indicated by the Examiner. Fig. 1 shows a structure with one unitary lumen (14) and two inlet holes (24, 26) and thus is distinct from two wells with a channel therebetween, as recited in claim 1. Since the embodiment of Fig. 1 does not disclose any channel, it also cannot disclose a channel that is formed as a through-hole in the top member.

Furthermore, Jarnigan discloses a number of sample receiving wells, such as 80, connected to subchamber 92 that receives a chemotactic agent, by capillaries 94. Since 92 is connected to all of the capillaries 94, the concentration of the chemotactic agent in each of the capillaries is the same, and a concentration gradient is only created along the length of the capillaries. Thus, Jarnigan does not have a first fluid stream with a first substance having a first concentration and a second fluid stream with a second substance having a second concentration. Furthermore, if the capillaries are considered to be the first fluid stream and the second fluid stream, they do not flow adjacent and parallel to each other without mixing, to create a dynamic concentration gradient, as recited in claim 1.

With respect to claim 17, as discussed above, Harrison does not disclose all the method steps of claim 17, and Jarnigan cannot cure this deficiency. Specifically, Jarnigan does not disclose the steps of disposing either a leukocyte migration mediator or endothelial cells in the channel and delivering a sample comprising leukocytes to the channel by laminar flow. Jarnigan simply mentions that leukocytes could be used but does not disclose how. Thus, neither Harrison or Jarnigan, alone or in combination, disclose all the limitations of method claim 17.

With respect to claim 1, as discussed above, the combination of Harrison and Jarnigan do not disclose all of the limitations and Jeon does not cure this deficiency. Claim 1 states that the housing has a base member and a top member and the at least one channel is formed as a through-hole in the top member. Jeon describes a base member (silicon wafer 200) with a cover member (PDMS replica 210), as shown in Figs. 5 and 6. The channels (fluid network 240) are clearly formed within the device, and thus are not formed as through-holes in the top member, as recited by claim 1.

With respect to claim 17, as discussed above, Harrison and Jarnigan do not disclose all the limitations of claim 17, and Jeon cannot cure this deficiency. Specifically, Jeon does not disclose the steps of disposing either a leukocyte migration mediator or endothelial cells in the channel and delivering a sample comprising leukocytes to the channel by laminar flow. Jeon does not disclose a system for monitoring leukocyte migration and thus fails to disclose leukocytes, endothelial cells or leukocyte migration mediators at all. Thus, neither Harrison or Jarnigan or Jeon, alone or in combination, disclose all the limitations of method claim 17.

Furthermore, there is no motivation to combine Harrison and Jeon to create a concentration gradient that is perpendicular to the direction of fluid flow. As discussed above, Harrison intends for the converging streams to mix and this is contrary to creating a concentration gradient perpendicular to the flow. The Examiner is using hindsight reasoning to combine these two references, which have the sole similarity of both being microfluidic devices.

For at least these reasons, Applicants submit that claims 1 and 17 (and all claims that depend therefrom) are not rendered obvious by the combination of Harrison, Jarnigan and Jeon and Applicants respectfully request withdrawal of this rejection.

Claim 8 stands rejected under 35 U.S.C. 103(a) as being allegedly rendered obvious by Harrison in view of Jarnigan in view of Jeon in further view of U.S. Patent No. 5,460,945 to Springer ("Springer"). As discussed above, Harrison does not teach a first and a second fluid stream having different concentrations, and flowing adjacent and parallel to each other without mixing, to create a dynamic concentration gradient, as stated in claim 1 and neither Jarnigan or Jeon makes up for this deficiency. Furthermore, a combination of all three references with Springer does not make up for this deficiency. Springer discloses a device and method for monitoring leukocyte rolling, however the device does not disclose the system or method as claimed. Springer's device is meant to be placed under a microscope and consists of a glass slide (42) with an inlet (54) and outlet (56) for introducing the blood or leukocytes. This device does not have a channel or two wells and cannot have a plurality of chambers or a channel formed as a through-hole in a top member. Furthermore, the device operates by placing a substance onto the slide and then introducing the leukocytes to watch the reaction. This device does not allow for laminar flow of two substances and does not even disclose introducing such substances, as claim 1 (and thus dependent claim 8) states. Furthermore, the device of Springer cannot create a dynamic concentration gradient as claimed. Thus, the combination of Harrison, Jarnigan, Jeon and Springer, if possible, would still not teach the device of claim 8. For at least these reasons, Applicants submit that claim 8 is not rendered obvious by the combination of Harrison, Jarnigan, Jeon and Springer, and Applicants respectfully request withdrawal of this rejection.

Claims 10 and 12-16 stand rejected under 35 U.S.C. 103(a) as being allegedly rendered obvious by Harrison in view of Jeon. Claims 10 and 12-16 are cancelled, thus this rejection is moot.

Double Patenting Rejection

The Examiner has provisionally rejected claims 1-7, 9-12 and 17 on the grounds of nonstatutory double patenting as being unpatentable over copending Application No. 10/688905 in view of Harrison. As these are provisional double patenting rejections, Applicants request that these rejections be held in abeyance until an indication of allowable subject matter has been made.

CONCLUSION

It is respectfully submitted that the present application is now in condition for allowance, which action is respectfully requested. The Examiner is invited to contact Applicants' representative to discuss any issue that would expedite allowance of the subject application.

Any fees for extension(s) of time or additional fees required in connection with the filing of this response, are hereby petitioned under 37 C.F.R. § 1.136(a), and the Commissioner is authorized to charge any such required fees or to credit any overpayment to Kenyon & Kenyon's Deposit Account No. 11-0600.

Respectfully submitted,

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